4:15

810-2 The First Five Years of the Qantas Cardiac Arrest Program

M.F. O'Rourke, E. Donaldson. *St Vincent's Hospital, Sydney, New South Wales, Australia, Qantas Airways, Sydney, Australia*

Controversy surrounds provision of defibrillators in commercial aircraft, with most carriers not equipped. From September 1, 1991 to August 1996, all 53 Qantas B747 and B767 international aircraft have carried Heartstart 3000 defibrillators, with cabin crew trained to handle cardiac arrest in conjunction with medical or paramedical volunteers, and with advice available by radio from Qantas physicians in Sydney. Over the five year period, the defibrillators were used on 87 occasions, 47 times for monitoring an acutely ill passenger, and 40 times for cardiac arrest. Twenty-two episodes of cardiac arrest occurred in aircraft, 6 in VF, 13 in asystole or IVR, 3 in sinus rhythm. VF was successfully terminated in 5, with 2 long-term survivors (33%). No shock was advised or delivered in the other 16. All with asystole or IVR died, and resuscitation was discontinued during flight in 15. All 3 with SR survived, but one died within 24 hours. Aircraft were diverted on 17 occasions. Eighteen episodes of cardiac arrest occurred in terminals; VF was the cause in 15 and SR in 2. Defibrillation was initially successful in all with VF, and 4 (27%) were long-term survivors. One with SR died within 24 hours.

Cardiac arrest in aircraft, though infrequent (87/million flight sectors, 0.72/million passengers on Qantas) is well handled, with acceptable long-term survival from VF, and through identification of other rhythms for which costly aircraft diversion can be avoided. The program adds to passenger safety, aids operational performance, and is justifiable on economic grounds.

4:30

810-3 Is it Necessary to "Miss" Acute Myocardial Infarction in the ER?

J.P. Ornato, M.A. Peberdy, R.L. Jesse, M.C. Kontos, C.S. Nicholson, S.A. Tombul, S. Griswold, C. Roberts, J. Tatum. *Virginia Commonwealth University/Medical College of Virginia, Richmond, VA, USA*

Five % of emergency room (ER) pts with acute myocardial infarction (AMI) are "missed" by emergency physicians and sent home inappropriately. To determine whether "missed" AMIs can be detected cost-effectively, we examined results of a critical pathway chest pain (CP) triage strategy using SPECT gated technetium 99m-sestamibi rest perfusion imaging to evaluate 1,494 consecutive ER CP pts with suspicious symptoms and a non-diagnostic ECG. The decision to admit CP pts judged "low risk" for AMI (Level 4) by ER physicians was based on the ER cardiac scan results. Pts with prolonged (>30 min) symptoms and a non-diagnostic ECG (Level 3) also received a cardiac scan followed by an 8-hour "r/o MI" observation protocol. *Results:*

Level	N	Age	Abnormal Scan	Admitted	AMI
3	461	56 ± 13	133 (30%)	449 (97%)	19
4	1033	48 ± 14	112 (11%)	155 (15%)	8

27 AMI pts with non-diagnostic initial ECGs were identified by the strategy. Posterior & lateral AMIs were most commonly missed one ECG and detected by the cardiac scan. Compared to pts treated in the year prior to the triage strategy, the % of Level 4 pts admitted decreased from >30% to 15%. Since a cardiac scan costs <15% of the cost of an overnight admission, the strategy is highly cost effective at our institution. We conclude that critical pathways including SPECT cardiac imaging can cost-effectively detect AMI cases that might be "missed" otherwise.

4:45

810-4 Resuscitation Course and Outcome After Early Defibrillation for Out-of-Hospital Ventricular Fibrillation

The Arrest Investigators. *University of Washington, Seattle, WA, USA*

Although considered the cornerstone of therapy for out-of-hospital ventricular fibrillation (VF), early defibrillation by EMT's has not universally improved survival from cardiac arrest. This may be because an apparent benefit in some patients (Pts) is compensated by a lack of benefit or even harm in others. To address this concern, 386 consecutive Pts with nontraumatic VF were evaluated for their response to-, and factors predicting the outcome of- early defibrillation. All patients were defibrillated, and then treated by standard ACLS guidelines. In group 1 (n = 42), ≤ 3 (mean 1.5) shocks resulted in asystole/PEA, all of whom died in the field. Group 2 (n = 111) responded to ≤ 3 shocks with an organized rhythm/pulse (ROSC), which was sustained to hospital in 96%. Group 3 (n = 221) required >3 shocks for refractory VF, in 41% of whom ROSC was sustained to hospital. Groups were compared by arrest location (public vs not), whether witnessed, receipt of bystander CPR, initial VF amplitude, and time from dispatch to BLS arrival.

Group	Age (yrs)	Men	Public	Witnessed	CPR	VF Amplitude	BLS Time
1	67	77%	21%*	45%*	42%*	0.3 mV*	4.3 min
2	68	80%	43%	81%	61%	0.5 mV	4 min
3	65	82%	50%	86%	63%	0.4 mV	4.2 min
p*	NS	NS	0.055	0.001	0.01	0.03	NS

Pts responsive to ≤ 3 shocks were similar to those needing >3 shocks, despite differences in outcome. Asystole/PEA after ≤ 3 shocks was an ominous marker of poor outcome, associated with low amplitude VF, and with surrogates of its presence for a protracted time before treatment. Pts respond differently to shock. In some, survival may be poor regardless of treatment, or even worsened if early shock displaces VF with asystole/PEA.

811 Basic Electrophysiology: Calcium Currents

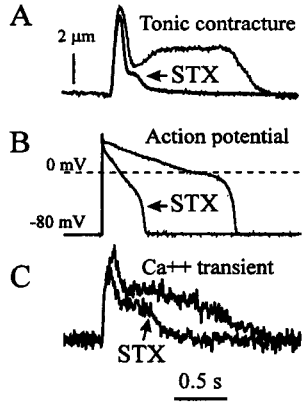
Wednesday, March 19, 1997, 4:00 p.m.–5:00 p.m.
Anaheim Convention Center, Room A10

4:00

811-1 Sarcolemma-Related Abnormalities of Excitation-Contraction Coupling in Cardiomyocytes from Dogs with Heart Failure

V.A. Maltsev, H.N. Sabbah, S. Goldstein, M. Lesch, A.I. Undrovinas. *Henry Ford Heart and Vascular Institute, Detroit, MI, USA*

The cellular mechanisms of impaired contractility were studied in chronic heart failure (HF) induced in dogs (n = 9) by multiple sequential intracoronary embolization with microspheres. Action potentials were measured in isolated LV cardiomyocytes by perforated patch clamp and Ca^{++} transients by fluo 3 probe. Contractions were recorded by edge movement detector in 425 field-paced (0.2 Hz) HF cardiomyocytes at $[Ca]_0$ = 1.2 mM. We found abnormal contractions in 53% of HF cardiomyocytes exhibiting a twitch followed by a tonic contracture (Fig. A). The tonic contracture coincided with a sustained plateau of action potential (Fig. B) and of Ca^{++} transient (Fig. C). Partial blockade of sarcolemmal Na^+ channel by a specific blocker saxitoxin (STX, 10 nM) or of L-type Ca^{++} channels by nifedipine (0.5 μM, not shown) reduced duration of both action potential (Fig. B) and Ca^{++} transient (Fig. C) and consequently abolished the tonic contracture (Fig. A).



These data suggest that abnormalities of contraction are mediated, in part, by modified sarcolemmal Na^+ and/or Ca^{++} channels in HF. We hypothesize that the steady-state inward current that we previously reported to occur in HF cardiomyocytes underlies both prolonged action potential and sustained Ca^{++} influx which in turn, produces Ca^{++} overload and cell contracture.

4:15

811-2 Cytoskeleton Disruption Results in Electromechanical Dissociation in Rat Ventricular Cardiomyocytes

A.I. Undrovinas, V.A. Maltsev. *Henry Ford Heart and Vascular Institute, Detroit, MI, USA*

The nature of the electromechanical dissociation (ED) syndrome found in patients with ischemic cardiac disease and myocardial infarction is still

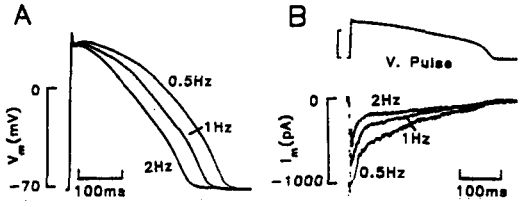
unknown. In the present study we tested a hypothesis that cytoskeleton breakdown can lead to ED. Effects of cytochalasin D (CytD), a disrupter of F-actin were assayed on the key processes consecutively involved in electro-mechanical coupling: action potentials (APs), L-type Ca^{++} current (I_{CaL}), Ca^{++} transients, and cell contractions measured in rat ventricular cardiomyocytes at 37ºC. The measurements were performed by using both perforated and whole-cell patch-clamp, fluo-3 Ca^{++} indicator, and an edge movement detector. In CytD-treated cells relaxation kinetics was slower and contraction amplitude was reduced (about twice at 0.8 μM of CytD). In addition, CytD slowed decay of Ca^{++} transients (τ_{decay} = 47.3 ± 2.8 ms, n = 20; in control cells: 28.1 ± 1.3 ms, n = 28, mean ± SEM, $p < 0.01$). The rising phase of Ca^{++} transients was also significantly slower in CytD treated cells (τ_{rise} = 5.1 ± 0.6 ms, n = 17; in control cells: 3.6 ± 0.2 ms, n = 21, $p < 0.01$). The suppressive effect of CytD on cell contractions could not result only from the changes in kinetics of Ca^{++} transient since the amplitude of the transient (442 ± 51 nM, n = 8) and resting Ca^{++} level (89.4 ± 7.3 nM) changed insignificantly (in control cells: 424 ± 38 nM and 91.4 ± 10.8 nM, respectively, n = 13). Moreover, at higher CytD concentrations (from 4 to 40 μM), contraction was totally blocked, but APs, I_{CaL}, and amplitude of Ca^{++} transient did not change resulting in a complete ED. We conclude that integrity of F-actin-based cytoskeleton is an important factor for EC coupling. Particularly, myofibrils can not properly respond to Ca^{++} transient when cytoskeleton is damaged. We speculate that disruption of the cytoskeleton reported in ischemia can have an implication for ED phenomena as well as for insufficient cardiomyocyte contractility shown in heart failure.

4:30

811-3 Action Potential Voltage-Clamp Reveals Important Contribution of Ca^{2+} Current to Rate-Dependent Changes in Human Ventricular Action Potentials

G.-R. Li, B. Yang, J. Feng, R.F. Bosch, S. Nattel. *Montreal Heart Institute, Montreal, Quebec, Canada*

Rate-dependent changes in the action potential (AP) are known to be an important determinant of arrhythmias. The mechanism of AP abbreviation at rapid rates in human ventricular myocytes is unknown: both Ca^{2+} (I_{Ca}) and K^+ currents are potential candidates. To determine the role of I_{Ca} in human ventricular AP control, cells were studied at 36ºC with whole-cell patch clamp technique. Inactivation and recovery of I_{Ca} were biexponential (eg, τ's of 8 ± 1 and 86 ± 10 ms at +10 mV; recovery τ's of 18 ± 3 and 174 ± 25 ms at −80 mV). AP duration at 90% repolarization (APD_{90}) decreased by 34 ± 2% when frequency was increased from 0.5 to 2 Hz (Fig. A). I_{Ca} block (200 μM Cd^{2+}) shortened APD and strongly inhibited rate-dependent changes in APD_{90} (to 5 ± 2%, $p < 0.01$ vs control). AP clamp was performed using action potentials recorded from the same cell at 0.5 Hz, and demonstrated important rate-dependence of Cd-sensitive I_{Ca} (Fig. B): peak I_{Ca} was decreased by 34 ± 4% from 0.5 to 2 Hz (1034 ± 134 to 690 ± 45 pA, $n = 5$, $p < 0.01$).



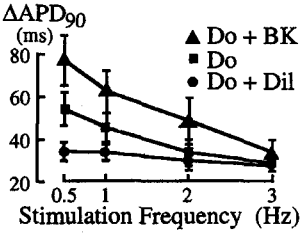
The results indicate that I_{Ca} is an important determinant of plateau duration, and point to a strong contribution of rate-dependent I_{Ca} inactivation to frequency-related changes in APD, which may play a major role in governing re-entrant ventricular arrhythmias in man.

4:45

811-4 The "Reverse-Use Dependence" of the New Class III Antiarrhythmic Dofetilide Can Be Modulated by Pharmacologic Agents Influencing $[Ca^{2+}]_i$

V. Gjini [1], S. Weyerbrock, M. Korth, J. Schreieck, C. Schmitt. *Klinikum rechts der Isar, Technische Universität, Munich, Germany,* [1] *Dept. Cardiol. Univ. Hosp. Center, Tirana, Albania*

The "reverse-use dependence" characterizing the antiarrhythmic effect of most currently used class III agents render their antiarrhythmic profile clinically unfavourable. This phenomenon is thought to be related, at least in part, to the accumulation of the not completely deactivated I_{Ks} (slow component of the delayed rectifier potassium channel), whose magnitude depends on $[Ca^{2+}]_i$. We tested the hypothesis that this phenomenon could be modulated by pharmacologic agents influencing $[Ca^{2+}]_i$. APD at 90% repolarization (APD_{90}) was determined in guinea-pig right ventricular papillary muscles by mean of standard microelectrode technique at stimulation frequencies 0.5, 1, 2 and 3 Hz, first in control and then 30 min after 10 nM dofetilide (Do). Thereafter, either 10 μM diltiazem (n = 10) (Dil), or 0.1 μM Bay K 8644 (n = 11) (BK) was added to the bath solution in order to decrease or increase $[Ca^{2+}]_i$. Measurements were repeated 30 and 20 min after Dil and BK, respectively.



The prolongation of APD_{90} (ΔAPD_{90}) under Do, Do + Dil and Do + BK (mean ± SEM) is shown in the following picture. The APD_{90} prolongation by Do was markedly reduced at high frequencies. This was more pronounced in the presence of BK, but was prevented by Dil.

Conclusion: The "reverse-use dependent" effect of the class III agent dofetilide can be modulated by pharmacologic agents influencing $[Ca^{2+}]_i$.

812 Echo–Contrast Studies of Myocardial Blood Flow and Perfusion

Wednesday, March 19, 1997, 4:00 p.m.–5:00 p.m.
Anaheim Hilton and Towers, Pacific B

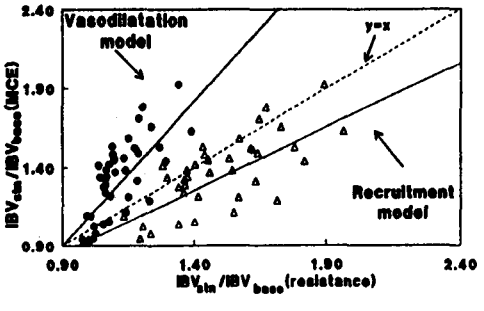
4:00

812-1 Myocardial Contrast Echocardiography Can Be Used to Quantify Intramyocardial Blood Volume: New Insights into Structural Mechanisms of Coronary Autoregulation

C.C. Wu, M.D. Feldman, J.D. Mills, D. Fischer, F.S. Villanueva. *University of Pittsburgh, Pittsburgh, PA, USA*

Changes in intramyocardial blood volume (IBV) mediate autoregulatory adaptations to coronary stenosis (STN). We tested the hypotheses that myocardial contrast echocardiography (MCE) could quantify changes in IBV in response to non-flow limiting coronary STN and that the relationship between coronary resistance- and MCE-derived IBV could yield insight into structural mechanisms of IBV change. The left anterior descending artery in 12 open chest dogs was instrumented with a flow probe, variable occluder, and intracoronary pressure catheter. MCE was performed using intra-aortic injection of Albunex during 3 to 5 non-flow-limiting coronary STN. IBV was derived using coronary resistance measurements applied to 2 theoretical models which assumed autoregulation to occur either via vasodilatation or microvascular recruitment. Flow was measured using radioactive microspheres, and MCE-determined IBV was calculated from microbubble transit rates.

At constant flow, MCE- and resistance- derived IBV were linearly related and increased with progressive STN (STN gradient 10–45 mmHg). MCE overestimated IBV derived by the vasodilatation model ($y = 1.84x - 0.76$, $p < 0.01$), and underestimated IBV calculated using the recruitment model ($y = 0.81x + 0.13$, $p < 0.01$) (Fig.).



MCE can quantify autoregulatory increases in IBV which maintain resting myocardial perfusion during coronary STN. Furthermore, these data suggest that both microvessel vasodilatation and recruitment simultaneously regulate IBV change. By detecting IBV heterogeneity, MCE may be a clinically useful technique for detecting and quantifying coronary disease under resting conditions.